

## Ambulatory electrocardiographic monitoring and the management of arrhythmias

### *Precision versus inflexibility*

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Although the technique for monitoring the ambulatory electrocardiogram was described by Holter 20 years ago, it was not adopted widely until the 1970's. Over the past five years or so, it has been used more and more as many indications for routine treatment depend on the information it provides. Clinical electrophysiology has not, however, become redundant, though it has often been developed by teams independent of those using the ambulatory electrocardiogram, who have not necessarily had the benefit of a sound electrophysiological understanding.

Conceptually, electrophysiology gives a measurement in milliseconds, while the ambulatory electrocardiogram provides a count of the extrasystoles. With regard to a specific event, electrophysiology is concerned with the why, whereas the ambulatory electrocardiogram is concerned with how many. Electrophysiology leads to a hypothesis as to the possible mechanism, while the ambulatory electrocardiogram results in statistically correct figures whose clinical application one is less likely to question.

One method should not take preference over the other. They should be complementary though this is not reflected in the published reports. It would be easy to make a case for either. In relation to the remarkable triumphs of surgery and cardiac pacing, electrophysiology has not fundamentally affected the medical treatment of the great majority of arrhythmias. On the other hand, it has been the limitations of the ambulatory electrocardiogram that we have chosen to study. Counting the events is not to be confused with grasping the problem, and the weight of figures should not lead to rigid opinions.

#### **Ambulatory electrocardiogram and mechanism of arrhythmias**

Published reports suggest that while ambulatory electrocardiography is well suited to counting events, it

plays no part in the study of their mechanism, in contrast to electrophysiology. This, however, is not the case. One daily example is that of paroxysmal junctional tachycardias; everything is known of their re-entry mechanism, yet nothing of the conditions governing their spontaneous appearance. Though repeated recordings, designed to capture the onset of these spontaneous bursts, are tedious to perform, they can be intelligently analysed to answer specific questions. Thus, one discovers they are triggered by extrasystoles, both atrial and ventricular, by sinus tachycardia, or by junctional escape. These events can then be adopted as therapeutic targets and they are often more amenable to treatment than re-entry block.

In applying the same approach to the onset of atrial fibrillation, one sees that electrophysiology has contributed little to their understanding, except that they can be artificially triggered. This information is of little therapeutic significance. The reports concerning the ambulatory electrocardiogram have not been orientated toward the mechanism of the onset of atrial fibrillation. It is, however, clear that this disturbance of rhythm can be secondary to either excessive vagal tone or sympathetic tone. This has long been established experimentally and there is a diversity of therapeutic measures. It is the role of the ambulatory electrocardiogram to uncover the clinical corollary of these facts, but not by counting the extrasystoles. Rather, it is to monitor continuously so that spontaneous events are recorded. Thus correlations can be established for the clinical circumstances associated with their onset (time of day, effort, or emotion) and with the important variable of sinus rate and its variations preceding the crisis.

The problem is more complex in the case of ventricular arrhythmias. In contrast to the two examples above, published reports on the subject are prolific. The real problems, however, are not touched on

except in an oversimplified manner. Paroxysmal ventricular tachycardia in the absence of premature extrasystoles is dismissed by the users of the ambulatory electrocardiogram and remains the province of the electrophysiologists with the well-known limitations of their methods of provocation. Being unable to study directly the tachycardias, the extrasystoles which are assumed to be their equivalent are studied in great detail, though this is far from proven. What is more alarming is that their equivalence is so rarely questioned. By analogy, it seems that the extrasystole that provokes a junctional tachycardia does not share the same mechanism. What is the evidence that it differs from the extrasystole that initiates a ventricular tachycardia, since it is proven that in certain cases an atrial extrasystole may play the same role? Nobody would conclude, having suppressed the extrasystoles medically which lead to junctional tachycardias, that the circuit itself had been blocked. Why then the different reasoning in relation to extrasystoles and ventricular tachycardias, on the basis of their morphological similarities?

As it is impractical to use the ambulatory electrocardiogram in cases of tachycardia, it has been widely used in the study of ventricular extrasystoles. It is in this field that many non-physiological, epidemiological studies have been carried out, with some disastrous consequences. There appears to be more emphasis on verifying the figures than on analysing their significance. When the day to day variation in the number of extrasystoles exceeds the confidence limits, it is concluded that the patient is not to be trusted and is rejected. Would it not be more important to establish the reasons for this? These are sometimes very straightforward, as when thresholds exist for the extrasystoles that appear with changes in sinus rate. The thresholds may be different in different cases. Yet again, the real correlation may be with the level of sympathetic activity, rather than with the basal sinus rate.

To elucidate these problems, one must abandon the simple counting of events. Only rarely can cause and effect be established by comparison of the number and incidence of extrasystoles with cardiac rate. A more detailed study, beat by beat, becomes necessary. It is an electrophysiological analysis that leads to an understanding of the results obtained from the ambulatory electrocardiogram.

In other words, the figures may be precise, but the conclusions drawn erroneous. When it is uncertain whether the events counted are truly equivalent, it is obvious that even the most reliable mathematical or statistical formulae should not be indiscriminately applied. In the province of arrhythmias, two plus two do not necessarily make four. It has not been shown that two extrasystoles that are isolated are comparable

to two that are coupled, since the mechanisms for each may be different. Likewise, an isolated extrasystole differs from another with respect to morphology, coupling, events leading to its appearance, etc.

There are probably fundamental reasons why the published reports become increasingly confused with each additional study of a purely quantitative nature whose conclusions are at best divergent and usually contradictory. The problem of the prognostic value of extrasystoles occurring after myocardial infarction is the most striking example. The diverse methods adopted for counting and grouping extrasystoles into different categories reflect the concern of the authors who have grasped these problems. It seems that the ambulatory electrocardiogram should be used more comprehensively in view of the disappointing results obtained by even the most rigorous analysis of figures, which otherwise do not take into account in many cases some commonsense variables like the presence or the absence of treatments with possible direct or indirect antiarrhythmic properties.

#### **Ambulatory electrocardiogram and efficacy of treatment**

The technique of the ambulatory electrocardiogram has made it possible to evaluate therapeutic effects in an objective manner, which was impossible before. This has eliminated the subjective factors that were a feature both of patients and doctors. Whereas subjective methods dealt with symptomatic arrhythmias which were both major and infrequent, the ambulatory electrocardiogram discloses also the asymptomatic arrhythmias which are minor and frequent, the extrasystoles. It seems the choice is between relieving the patient and satisfying the statistician. This alternative should not, however, be taken seriously since scientific method does not necessarily mean inflexible thinking. But the fact is that the published reports on new drugs tend to deal with tidy protocols or difficult patients, while protocols that cannot be faulted are not feasible when there are severe arrhythmias.

Review of the published papers during the last few years will show the paucity of publications on the subject of prophylactic treatment of major arrhythmias, whether they are atrial, junctional, or ventricular. Antiarrhythmics are categorised on the basis of the percentage reduction in the number of extrasystoles. One should not therefore be surprised that drugs selected on this basis, where minor arrhythmias have been abolished, do not provide the benefits expected when applied to the major clinical arrhythmias. It would not be difficult to find examples, as the procedures obviously exclude inactive drugs but do not clearly identify the most useful. Major arrhythmias often react differently from minor arrhythmias,

in ways that are sometimes unequal and unpredictable, since they represent either a more severe form of the same mechanism or another mechanism altogether.

Certain drugs have properties that render them unsuitable for the rigorous procedures of randomised, double blind cross-over trials. They thus prevent the use of strict methods of selection, as exemplified by the case of amiodarone. Light sensitivity in many cases precludes simple blind prescribing. Double blind prescribing would also be illusory since bradycardia occurs in addition to the problems of ventricular repolarisation. Controlled experiments using similar drugs are not possible since there are none. Crossing with a placebo is made difficult by the delayed action and its long half-life. Randomising the therapeutic sequences would entail allowing for the elimination of the drug which may take up to three months. It may be for these cumulative reasons that in countries with the strictest legislation, this drug has been accepted so slowly, despite its recognised merits as the quasi-ideal antiarrhythmic with the largest range.

The combination of two drugs leads to complex procedures, difficult to put into effect, as a result of the theoretical sequences which would be required. It may, however, be fallacious to suppose that a disturbance of rhythm must necessarily respond to one drug or another, rather than to both, whether separately or in combination. There are numerous examples, in particular the combination of local anaesthetic and beta blocker and/or amiodarone, or digitalis with quinidine, amiodarone, or verapamil. One can but conduct treatment openly; the results are no less reliable and the clinical value undiminished despite the difficulty in applying equations.

The principal problem is that of patient selection, which is more important than that of methods. Every experienced clinician knows that in the final analysis it is on him that an informed opinion of a new drug depends. It is extremely unusual that a valid opinion cannot be based on a dozen carefully chosen patients, later to be confirmed by a more formal procedure. It is naturally more difficult for a statistician to accept this approach than to formulate the rules which should theoretically be adopted.

It is certainly possible to reconcile subjective and objective methods, using the ambulatory electrocardiogram to confirm or invalidate, or at least to document, the effects of drugs on major arrhythmias. Choices have, however, to be made as it is impossible to constrain an arrhythmia to the limits of a procedure: it is the procedure that must sacrifice its absolute rigidity, depending on each case. One cannot always predict that a decrease in duration and frequency of paroxysms of atrial fibrillation occurring a

few times a month may assume clinical significance; nor can one suppose that the ambulatory electrocardiogram will be of more value than the evidence of the patient. For both ethical and practical reasons, it would be difficult to ask a patient to take drugs of unknown efficacy when he had syncopal tachycardias. The effect of a drug on a major arrhythmia, usually in the presence of heart disease, should be closely monitored, not only because there are attendant risks, but also because it may not be straightforward to establish whether a therapeutic policy should be adopted sooner or later than anticipated.

## Conclusions

The notion that electrophysiology, as an approach to the understanding of the mechanisms of cardiac arrhythmias, should be in opposition to the ambulatory electrocardiogram, aimed mainly at counting events, must surely be reviewed. A simple example illustrates that there are two possible ways to use the 24 hour electrocardiogram. Let us imagine that there is a group of patients with ventricular extrasystoles for which the common factor is their number in 24 hours, ignoring their incidence, morphology, coupling, grouping, or causal cardiac pathology. If this group of extrasystoles (rather than patients) is treated alternately by local anaesthetics and beta blockers, the drug which is shown statistically to be most beneficial will not necessarily be of practical clinical significance. In the first place, account is not taken of the mechanism of the arrhythmia and in the second place, account is not taken of the pharmacological properties of the drugs. What is of interest, is to determine which extrasystoles in which patients are influenced in which manner and by what drug. Thus, the nature and origin of a rhythm disturbance that is apparently homogeneous can be more readily elucidated. Given the same data, the interpretation of the results will have very different consequences for an understanding of these extrasystoles and a therapeutic approach to them. We feel it is important that due thought be given to these problems, without which the 24 hour electrocardiographic method is at risk of being unnecessarily depreciated.

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